Journal of Pioneering Medical Sciences
Received: July 22, 2025 | Accepted: August 13, 2025 | Published: September 05, 2025
Volume 14, Issue S02, Pages 223-230

DOI https://doi.org/10.47310/jpms202514S0234

Clinical and Autoantibody Profile of Systemic Sclerosis Patients in Saudi Arabia: A Single-Center Retrospective Study

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Abstract **Objectives: Background:** Systemic Sclerosis (SSc) is a rare autoimmune disease with significant ethnic and geographic variability. Autoantibody patterns and organ involvement influence prognosis. Data on SSc from Saudi Arabia are scarce. To describe the clinical presentation, autoantibody profile and organ involvement of Saudi SSc patients and to explore associations between autoantibodies and Interstitial Lung Disease (ILD). **Methods:** We conducted a retrospective observational study at a single tertiary hospital in Saudi Arabia. Adult patients fulfilling the 2013 ACR/EULAR classification criteria for SSc between 2015-2024 were included. Demographic, clinical and serologic data were extracted from medical records. Associations between SSc subtypes, antibody profiles and ILD were analyzed. **Results:** Twenty-one patients were included (95.2% female; mean age 50.0±13.4 years; mean age at disease onset 33.7±10.4 years). Diffuse cutaneous SSc (dcSSc) accounted for 76.2% and limited cutaneous SSc (lcSSc) for 23.8%. Common manifestations included gastroesophageal reflux disease (95.2%), Raynaud's phenomenon (90.5%), sclerodactyly (90.5%) and ILD (76.2%). Autoantibodies were frequent: ANA (95.2%), anti-topoisomerase I (ATA, 57.1%) and Anti-Centromere (ACA, 10%). ILD was strongly associated with dcSSc (100% vs. 0% in lcSSc, $p<0.001$) and trended toward association with ATA positivity (91.7% vs. 8.3%, $p = 0.055$). All ACA-positive patients ($n = 2$) were ILD-negative. **Conclusion:** This first Saudi cohort demonstrates a younger age at diagnosis and a high prevalence of ILD compared to international reports. ATA was associated with ILD, while ACA appeared absent among ILD cases. Given the very small sample size, these findings should be considered hypothesis-generating and warrant confirmation in larger, multicenter studies.

Key Words Systemic Sclerosis, Scleroderma, Interstitial Lung Disease, Anti-Topoisomerase I, Anti-Centromere Antibody

INTRODUCTION

Fibrosis, vasculopathy and the generation of autoantibodies are the hallmarks of systemic sclerosis (SSc), a chronic inflammatory illness. Based on the degree and location of skin involvement, SSc is divided into two categories: diffuse cutaneous SSc (dcSSc) and limited cutaneous SSc (lcSSc). Systemic sclerosis is regarded as a rare disease globally, with an incidence of 100 to 300 cases per million people [1]. The prevalence and severity of systemic sclerosis differ among different racial and ethnic groupings, despite the fact that the disease affects people of all races and geographical locations. The estimated prevalence of SSc in Europe ranged from 7.1 to 15.8 cases per 100,000, whereas in the United States it was 24.2 cases per 100,000 [2]. For Arab countries, the data is scarce and vary depending on the study sample. To our knowledge, there is no data available for systemic sclerosis prevalence in Saudi Arabia.Clinical features of SSc are miscellaneous. Thoughskin, vascular, gastrointestinal and lungs are commonly involved organs,musculoskeletal,renal, cardiac are also involved [3]. Local data showed that pulmonary arterial hypertension developed in about 70% of SSc patients and it was the leading cause of mortality [4]. About 90 percent of patients with SSc develop gastrointestinal manifestations [5]. Dysphagia, heartburn and diarrhea were the common symptoms. The primary clinical symptom of vascular dysfunction in Systemic Sclerosis (SSc) is Raynaud phenomenon, characterised by sequential colour changes in the digits triggered by cold, stress, or temperature fluctuations. lcSSc is frequently linked to CREST syndrome, which encompasses calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly and telangiectasia. Serological markers in patients with systemic sclerosis exhibit variability; certain antibodies, such as anti-topoisomerase I and anti-centromere, are important in delineating clinical characteristics of the disease and offer

prognostic significance. Anti-Centromere (ACA), Anti-Topoisomerase I (ATA), anti-RNA polymerase III, anti-fibrillarin, anti-Th/To and anti-PDGFR are autoantibodies associated with systemic sclerosis. Scleroderma may lead to significant morbidity and mortality in specific populations, especially when substantial skin involvement, cardiac and/or pulmonary complications, renal disease and the existence of anti-topoisomerase I antibodies and/or anti-Th/To antibodies are present. Male sex and a younger age at disease beginning may be correlated with heightened mortality.Indeed, SSc disease manifestations and survival time has been reported recently to be affected by ethnicity [11]. Moreover, the ethnicity background partially contributed the varieties of reports that indicate presence of association between the involvement of organ and each antibody [12]. Due to the scarcity of data about systemic sclerosis in Arab countries, especially in Saudi Arabia, further studies are needed to clarify more about the clinical and laboratory profile. We aimed to assess the clinical and autoantibody profile of SSc patients in a Saudi cohort. We hope this work will add to the local data and literature and improve our understanding to SSc.

Objectives

The study aimed:

- To assess the demographic, clinical and serological characteristics of Saudi patients with SSc
- To compare clinical manifestations between diffuse and limited SSc subtypes
- To evaluate the prevalence of interstitial lung disease and its association with autoantibody patterns
- To contribute baseline data for future national and regional SSc research

MATERIALS AND METHODS

The study cohort comprised all adult patients with SSc who were followed regularly at the Rheumatology clinic from 2015 to 2024 at King Saud Hospital, Qassim, Saudi Arabia. All included patients fulfilled the criteria of American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) [13]. Their antibody profiles and clinical features, including age, sex, disease duration, organ involvements [skin, Gastrointestinal Tract (GI), lungs, heart, kidneys, Scleroderma Renal Crisis (SRC) and Pulmonary Arterial Hypertension (PAH)] and overlap with CTD, were obtained from medical records. Our institutional ethics committee and the research advisory council approved the study. DcSSc was characterised by skin involvement proximal to the elbows and knees, whereas lcSSc indicated skin involvement distal to the elbows and knees or impacting the face at least two years post-onset of SSc. Gastrointestinal involvement was characterised by gastro-oesophageal reflux disease, dysphagia and bacterial overgrowth necessitating antibiotics. Lung involvement was characterised by bibasal pulmonary fibrosis identified through chest radiography or computed tomography. Heart involvement was characterised by a left ventricular ejection fraction of less than 40%, ascertained through echocardiography, the presence of conduction disturbances or arrhythmias necessitating treatment, or the occurrence of congestive heart failure. SRC was characterised by the presence of malignant arterial hypertension (diastolic blood pressure exceeding 120 mm Hg accompanied by grade III or IV hypertensive fundoscopic alterations as per the Keith-Wagener classification) or swiftly advancing oliguric renal failure without identifiable aetiologies during the progression of SSc [16].

SSc may potentially lead to chronic renal illness characterised by high blood creatinine levels or proteinuria, independent of SRC. Renal involvement was characterised by current or historical SRC, together with persistent proteinuria or a glomerular filtration rate of less than 60 ml/min per 1.73 m². Pulmonary Arterial Hypertension (PAH) was diagnosed based on a mean pulmonary arterial pressure over 25 mm Hg, ascertained through direct right heart catheterisation, or an estimated pulmonary arterial pressure beyond 30 mm Hg, derived from tricuspid flow velocity using Doppler echocardiography. The diagnosis of overlapping connective tissue disease was established based on the subsequent criteria: SLE or RA were diagnosed based on the 1982 or 1987 criteria established by the American College of Rheumatology, respectively [22,23]. Sjögren's syndrome was diagnosed in accordance with the 1999 Ministry of Health and Welfare's Diagnostic Criteria for SS. Myositis is characterised by inflammation of skeletal muscle, indicated by a blood Creatine Kinase (CK) level exceeding the normal institutional range (247 IU/l for men or 170 IU/l for women). Other illnesses linked to elevated serum CK levels were excluded, including myocardial infarction, muscular dystrophy, circulatory problems, hypothyroidism and drug-induced myopathy. Myositis encompassed muscle involvement resulting from Systemic Sclerosis (SSc), as well as polymyositis or dermatomyositis aggravated by SSc. All diagnoses were established retrospectively and validated by the data in medical records. The commencement of Systemic Sclerosis (SSc) was characterised by the emergence of Raynaud's phenomenon and/or joint symptoms prior to skin sclerosis, along with the manifestation of distinctive symptoms resulting from organ involvement [25].

Autoantibody Tests

Patient sera were analysed for Antinuclear Antibodies (ANA) via indirect immunofluorescence employing HEp-2 cells as the antigen substrate (Antibodies, Davis, CA, USA). ATA and anti-U1RNP were identified using passive immunodiffusion utilising calf thymus extracts (INOVA Diagnostics). Antinuclear Antibodies (ACA) were assessed using indirect immunofluorescence utilising HEp-2 cells.

Statistical Analysis

The results expressed as the mean ± Standard Deviation (SD) for continuous variables and percentages for categorical variables. The p value of <0.05 was considered significant. The variables compared using 2-sample t-tests, chi-square tests and Fisher's exact tests. The statistical program Epi Info™ 3.5.4 was used in the analysis.

RESULTS

The study included 21 SSc patients with a mean age of 50.0±13.4 years and a mean age of disease onset of 33.7±10.4 years. The majority were female (95.2%) and all were Saudi nationals. Regarding comorbidities, 19.0% had diabetes, 38.1% had hypertension, 4.8% had Chronic Kidney Disease (CKD), 33.3% had dyslipidemia, 38.1% had hypothyroidism and 9.5% had a history of cancer (Table 1).

Among the 21 patients with SSc, the most common clinical manifestations were Gastroesophageal Reflux Disease (GERD) (95.2%), Raynaud's phenomenon (90.5%), sclerodactyly (90.5%), dysphagia (90.5%) and Interstitial Lung Disease (ILD) (76.2%); almost, half of them had Nonspecific Interstitial Pneumonia (NSIP) picture in HRCT. Fatigue was also highly reported (81.0%), while weight loss (38.1%) and pulmonary hypertension (38.1%) were present in over a third of cases. Joint involvement occurred in 47.6% of patients and telangiectasia in 52.4%. Less frequent features included digital ulcers (33.3%), calcinosis (19.0%), thromboembolic events (19.0%), cardiac involvement (14.3%) and autoimmune overlaps such as Sjögren's syndrome (14.3%), rheumatoid arthritis (4.8%) and myopathy (4.8%) (Table 2).

Laboratory findings among SSc patients is given in Table 3. Majority had elevated Erythrocyte Sedimentation Rate (ESR) (71.4%) and positive Antinuclear Antibodies (ANA) (95.2%), with speckled (40.0%) and homogeneous (30.0%) being the most common ANA patterns. Over half of the patients (57.1%) tested positive for anti-topoisomerase I antibodies, while 19.0% had anti-dsDNA positivity. Other autoantibodies were less prevalent, including anti-Ro/SSA (23.8%), rheumatoid factor (14.3%), antiphospholipid antibodies (33.3).

In the comparison of ILD prevalence among scleroderma patients, diffuse scleroderma subtype was significantly associated with ILD, with all diffuse cases (100%) presenting ILD and all limited cases free of ILD ($p<0.001$), highlighting disease subtype as a major determinant. The presence of certain ANA patterns was also significantly associated with ILD. The centromere pattern was seen only in non-ILD patients (100%), whereas speckled (100%) and mixed patterns (100%) were exclusive to ILD cases ($p = 0.026$). Although not statistically significant, anti-topoisomerase I (Scl-70) positivity was more frequent among ILD patients (91.7% vs. 8.3%, $p = 0.055$), suggesting a strong trend. Other clinical features such as Raynaud's phenomenon, digital ulcers, telangiectasia, GERD and thromboembolic events were more common in ILD cases, but not statistically significant. Dysphagia, despite showing higher prevalence in ILD patients (73.7%), did not reach significance in this version ($p = 0.406$). No statistically significant differences were observed in anti-dsDNA, anti-Smith, RF, antiphospholipid, anti-Ro/SSA, anti-La/SSB, anti-CCP antibodiesbetween ILD and non-ILD patients (Table 4).

Table 1: Patients' Demographics and Comorbidities

Variables		N	%
Age (mean ± SD)	50.0±13.4 years		
Age of onset (mean ± SD)	33.7±10.4 years		
Gender	Male	1	4.8
	Female	20	95.2
Nationality	Saudi	21	100
	Non-saudi	0	0
Marital status	Single	7	33.3
	Married	14	66.7
Diabetes	No	17	81.0
	Yes	4	19.0
Hypertension	No	13	61.9
	Yes	8	38.1
CKD	No	20	95.2
	Yes	1	4.8
Dyslipidemia	No	14	66.7
	Yes	7	33.3
Hypothyroidism	No	13	61.9
	Yes	8	38.1
Cancer	No	19	90.5
	Yes	2	9.5

Table 2: Clinical Manifestations of Systemic Sclerosis

Clinical Manifestations	N	%
Fatigue	17	81.0
Fever	0	0
Weight loss	8	38.1
Skin thickening	21	100.0
Raynaud's phenomenon	19	90.5
Digital ulcers	7	33.3
Sclerodactyly	19	90.5
Telangiectasia	11	52.4
Calcinosis	4	19.0
Joint involvement	10	47.6
Gastroesophageal Reflux Disease (GERD)	20	95.2
Dysphagia	19	90.5
Pulmonary hypertension	8	38.1
Interstitial Lung Disease (ILD)	16	76.2
Cardiac involvement	3	14.3
Pericarditis	2	9.5
Myocarditis	2	9.5
Thromboembolic events	4	19.0
Scleroderma renal crisis	0	0
Overlap syndrome	4	19.0
Rheumatoid Arthritis (RA)	1	4.8
Systemic Lupus Erythematosus (SLE)	0	0
Myopathy	1	4.8
Sjögren's syndrome	3	14.3
Mixed Connective Tissue Disease (MCTD)	0	0

In the comparison between limited and diffuse scleroderma, patients with the diffuse subtype were generally diagnosed at a younger age (32.6 vs. 37.4 years) and had a shorter disease duration (15.2 vs. 19.8 years), though neither difference reached statistical significance. Clinical features such as Raynaud's phenomenon, digital ulcers, telangiectasia, GERD, dysphagia and thromboembolic events were more common in the diffuse group, but without significant statistical differences. ANA positivity was high in both groups; however, the ANA pattern showed a significant difference ($p = 0.017$), with centromere pattern seen only in limited cases and speckled pattern exclusive to diffuse cases.

Table 3: Laboratory Findings in Patients with Systemic Sclerosis

Laboratory Parameter	Category	N	%
Elevated Erythrocyte Sedimentation Rate (ESR)	No	6	28.6
	Yes	15	71.4
Elevated C-Reactive Protein (CRP)	No	20	95.2
	Yes	1	4.8
Antinuclear Antibodies (ANA)	Negative	1	4.8
	Positive	20	95.2
ANA Pattern (n = 18)	Centromere	2	10.0
	Homogeneous	6	30.0
	Nucleolar	3	15.0
	Speckled	8	40.0
	Mixed	1	5.0
Anti-topoisomerase I Antibodies	Negative	9	42.9
	Positive	12	57.1
Anti-double-stranded DNA Antibodies (Anti-dsDNA)	Negative	17	81.0
	Positive	4	19.0
Anti-Smith Antibodies	Negative	20	95.2
	Positive	1	4.8
Anti-U1 RNP Antibodies	Negative	21	100.0
	Positive	0	0.0
Rheumatoid Factor (RF) Antibodies	Negative	18	85.7
	Positive	3	14.3
Antiphospholipid Antibodies	Negative	14	66.7
	Positive	7	33.3
Anti-Ro/SSA Antibodies	Negative	16	76.2
	Positive	5	23.8
Anti-La/SSB Antibodies	Negative	20	95.2
	Positive	1	4.8
Anti-Cyclic Citrullinated Peptide (Anti-CCP)	Negative	20	95.2
	Positive	1	4.8

Table 4: Comparsion of ILD Prevalence with Patient Characteristics

Variable		ILD			
		No	Yes	Total	p-value
Age at diagnosis (years)		37.4±9.34	32.63±10.7	50.0±13.4	0.385
Disease duration (years)		19.8±9.2	15.18±4.6	33.7±10.4	0.145
Scleroderma type	Limited	5 (100.0%)	0 (0.0%)	5 (100.0%)	<0.001
	Diffuse	0 (0.0%)	16 (100%)	16 (100.0%)	
Raynaud's phenomenon	No	1 (50.0%)	1 (50.0%)	2 (100.0%)	0.361
	Yes	4 (21.1%)	15 (78.9%)	19 (100.0%)	
Digital ulcers	No	2 (14.3%)	12 (85.7%)	14 (100.0%)	0.147
	Yes	3 (42.9%)	4 (57.1%)	7 (100.0%)	
Telangiectasia	No	1 (10.0%)	9 (90.0%)	10 (100.0%)	0.157
	Yes	4 (36.4%)	7 (63.6 %)	11 (100.0%)	
Gastroesophageal reflux disease (GERD)	No	0 (0.0%)	1 (100.0%)	1 (100.0%)	0.567
	Yes	5 (25.0%)	15 (75.0%)	20 (100.0%)	
Dysphagia	No	0 (0.0%)	2 (100.0%)	2 (100.0%)	0.406
	Yes	5 (26.3%)	14 (73.7%)	19 (100.0%)	
Thromboembolic events	No	3 (17.6%)	14 (82.4%)	17 (100.0%)	0.172
	Yes	0 (0.0%)	4 (100.0%)	4 (100.0%)	
Elevated Creatinine	No	4 (20.0%)	16 (80.0%)	20 (100.0%)	0.067
	Yes	1 (100.0%)	0 (0.0%)	1 (100.0%)	
Elevated ESR	No	1 (16.6%)	5 (83.3%)	6 (100.0%)	0.627
	Yes	4 (26.7%)	11 (73.3%)	15 (100.0%)	
Elevated CRP	No	4 (20.0%)	16 (80.0%)	20 (100.0%)	0.067
	Yes	1 (100.0%)	0 (0.0%)	1 (100.0%)	
ANA	Negative	0 (0.0%)	1 (100.0%)	1 (100.0%)	0.567
	Positive	5 (25.0%)	15 (75.0%)	20 (100.0%)	
ANA Pattern	Centromere	2 (100.0%)	0 (0.0%)	2 (100.0%)	0.026
	Homogeneous	1 (16.7%)	5 (83.3%)	6 (100.0%)	
	Nucleolar	2 (66.7%)	1 (33.3%)	3 (100.0%)	
	Speckled	0 (0%)	8 (100%)	8 (100.0%)	
	Mixed	0 (0.0%)	1 (100%)	1 (100.0%)	
Anti-topoisomerase I antibodies	Negative	4 (44.4%)	5 (55.6%)	9 (100.0%)	0.055
	Positive	1 (8.3%)	11 (91.7%)	12 (100.0%)	
Anti-dsDNA antibodies	Negative	4 (23.5%)	13(76.5%)	17 (100.0%)	0.950
	Positive	1 (25.0%)	3 (75.0%)	4 (100.0%)	
Anti-Smith antibodies	Negative	5 (25.0%)	15 (75.0%)	20 (100.0%)	0.567
	Positive	0 (0.0%)	1 (100.0%)	1 (100.0%)	
Rheumatoid factor	Negative	5 (27.8%)	13 (72.2%)	18 (100.0%)	0.296

Table 4: Continue

	Positive	0 (0.0%)	3 (100.0%)	3 (100.0%)	
Antiphospholipid antibodies	Negative	2 (28.6%)	10 (71.4%)	14 (100.0%)	0.469
	Positive	1 (14.3%)	6 (85.7%)	7 (100.0%)	
Anti-Ro/SSA	Negative	5 (31.3%)	11 (68.8%)	16(100.0%)	0.152
	Positive	0 (0%)	5 (100%)	5 (100.0%)	
Anti-La/SSB	Negative	5 (25.0%)	15 (75.0%)	20 (100.0%)	0.567
	Positive	0 (0.0%)	1 (100.0%)	1 (100.0%)	
Anti-CCP	Negative	5 (25.0%)	15 (75.0%)	20 (100.0%)	0.567
	Positive	0 (0.0%)	1 (100.0%)	1 (100.0%)	
	Low	0 (0.0%)	1 (100.0%)	1 (100.0%)	

Table 5: Comparison of Demographics, Clinical Manifestations, Serological Markers and Treatment Modalities Between Limited and Diffuse Systemic sclerosis Patients

		Type of Scleroderma			
Variable		Limited	Diffuse	Total	p-value
Age at diagnosis (years)		37.4±9.34	32.63±10.7	50.0±13.4	0.385
Disease duration (years)		19.8±9.2	15.18± 4.6	33.7±10.4	0.145
Raynaud's phenomenon	No	1 (50.0%)	1 (50.0%)	2 (100.0%)	0.361
	Yes	4 (21.1%)	15 (78.9%)	19 (100.0%)	
Digital ulcers	No	2 (14.3%)	12 (85.7%)	14 (100.0%)	0.147
	Yes	3 (42.9%)	4 (57.1%)	7 (100.0%)	
Telangiectasia	No	1 (10.0%)	9 (90.0%)	10 (100.0%)	0.157
	Yes	4 (36.4%)	7 (63.6%)	11 (100.0%)	
GERD	No	0 (0.0%)	1 (100.0%)	1 (100.0%)	0.567
	Yes	5 (25.0%)	15 (75.0%)	20 (100.0%)	
Dysphagia	No	0 (0.0%)	2 (100.0%)	2 (100.0%)	0.406
	Yes	5 (26.3%)	14 (73.7%)	19 (100.0%)	
Thromboembolic events	No	3 (17.6%)	14 (82.4%)	17 (100.0%)	0.172
	Yes	2 (50.0%)	2 (50.0%)	4 (100.0%)	
Elevated Creatinine	No	4 (20.0%)	16 (80.0%)	20 (100.0%)	0.067
	Yes	1 (100.0%)	0 (0.0%)	1 (100.0%)	
Elevated ESR	No	1 (16.7%)	5 (83.3%)	6 (100.0%)	0.627
	Yes	4 (26.7%)	11 (73.3%)	15 (100.0%)	
Elevated CRP	No	4 (20.0%)	16 (80.0%)	20 (100.0%)	0.067
	Yes	1 (100.0%)	0 (0.0%)	1 (100.0%)	
ANA	Negative	0 (0.0%)	1 (100.0%)	1 (100.0%)	0.567
	Positive	5 (25.0%)	15 (75.0%)	20 (100.0%)	
ANA Pattern	Centromere	2 (100.0%)	0 (0.0%)	2 (100.0%)	0.017
	Homogeneous	1 (16.7%)	5 (83.3%)	6 (100.0%)	
	Nucleolar	2 (66.7%)	1 (33.3%)	3 (100.0%)	
	Speckled	0 (0.0%)	8 (100.0%)	8 (100.0%)	
	Mixed	0 (0.0%)	1 (100.0%)	1 (100.0%)	
Anti-topoisomerase I antibodies	Negative	4 (44.4%)	5 (55.6%)	9 (100.0%)	0.055
	Positive	1 (8.3%)	11 (91.7%)	12 (100.0%)	
Anti-dsDNA antibodies	Negative	4 (23.5%)	13 (76.5%)	17 (100.0%)	0.950
	Positive	1 (25.0%)	3 (75.0%)	4 (100.0%)	
Anti-Smith antibodies	Negative	5 (25.0%)	15 (75.0%)	20 (100.0%)	0.567
	Positive	0 (0.0%)	1 (100.0%)	1 (100.0%)	
Rheumatoid factor	Negative	5 (27.8%)	13 (72.2%)	18 (100.0%)	0.296
	Positive	0 (0.0%)	3 (100.0%)	3 (100.0%)	
Antiphospholipid antibodies	Negative	4 (28.6%)	10 (71.4%)	14 (100.0%)	0.469
	Positive	1 (14.3%)	6 (85.7%)	7 (100.0%)	
Anti-Ro/SSA	Negative	5 (31.3%)	11 (68.8%)	16 (100.0%)	0.152
	Positive	0 (0.0%)	5 (100.0%)	5 (100.0%)	
Anti-La/SSB	Negative	5 (25.0%)	15 (75.0%)	20 (100.0%)	0.567
	Positive	0 (0.0%)	1 (100.0%)	1 (100.0%)	
Anti-CCP	Negative	5 (25.0%)	15 (75.0%)	20 (100.0%)	0.567
	Positive	0 (0.0%)	1 (100.0%)	1 (100.0%)	
	Low	0 (0.0%)	1 (100.0%)	1 (100.0%)	
Steroid use	No	2 (50.0%)	2 (50.0%)	4 (100.0%)	0.172
	Yes	3 (17.6%)	14 (82.4%)	17 (100.0%)	
Cyclophosphamide	No	4 (30.8%)	9 (69.2%)	13 (100.0%)	0.340
	Yes	1 (12.5%)	7 (87.5%)	8 (100.0%)	
Mycophenolate mofetil (MMF)	No	4 (28.6%)	10 (71.4%)	14 (100.0%)	0.469
	Yes	1 (14.3%)	6 (85.7%)	7 (100.0%)	
Azathioprine	No	5 (33.3%)	10 (66.7%)	15 (100.0%)	0.105
	Yes	0 (0.0%)	6 (100.0%)	6 (100.0%)	
Methotrexate	No	4 (20.0%)	16 (80.0%)	20 (100.0%)	0.067
	Yes	1 (100.0%)	0 (0.0%)	1 (100.0%)	
Rituximab	No	5 (26.3%)	14 (73.7%)	19 (100.0%)	0.406
	Yes	0 (0.0%)	2 (100.0%)	2 (100.0%)	
Immunoglobulin	No	5 (25.0%)	15 (75.0%)	20 (100.0%)	0.567
	Yes	0 (0.0%)	1 (100.0%)	1 (100.0%)	
Proton pump inhibitor (PPI)	No	0 (0.0%)	2 (100.0%)	2 (100.0%)	0.406
	Yes	5 (26.3%)	14 (73.7%)	19 (100.0%)	

Although not statistically significant, anti-topoisomerase I antibodies (Scl-70) were more frequently positive in diffuse scleroderma (91.7%) compared to limited (8.3%), suggesting a potential association (p = 0.055). Other serological markers, including anti-dsDNA, anti-Smith, anti-RNP, anti-Ro, anti-La and anti-CCP, were more prevalent in diffuse patients but did not reach significance. Similarly, treatments such as steroids, cyclophosphamide, MMF, azathioprine and rituximab were more commonly used in diffuse cases. Methotrexate was only used in the limited group, while immunoglobulin and PPI use was seen exclusively in diffuse cases (Table 5).

DISCUSSION

This is a first descriptive retrospective cohort study of SSc patients in Saudi Arabia. The relatively small sample size is basically because of the rarity of the disease. Previous studies done for SSc patients in gulf region as well as the Asian and African populations showed a considerable variation in the sample size too [26-28]. Despite a small cohort, this study holds a significant contribution to SSc local data, as it is the first comprehensive study give insights about the clinical and autoantibodies profile in the Saudi Arabia.

Our study revealed a similar age of the patients at the onset of disease manifestations to SSc patients in Qatar, but in contrast to other Asian and European cohorts. Specifically, the mean age at initial manifestation of the disease in our participants was 33.7±10.4.This contrast to reported ages in averages of 42±13.4 years in Malaysian study, 47±0.7 years in a Japanese study and 45±15.2 years in a Spanish study [29,30,12,26]. Variations in female to male ratio in SSc has been reported in different ethnicities [31]. However, female predominance is a consistent finding, like in our study.

According to the skin involvement and the autoantibodies, the SSc is classified into diffuse and limited. In our study, the dcSSc was the predominant type. This is consistent with Qatar cohort [26]. Interestingly, the Japanese and Malaysian cohorts declared that occurrence of LcSSc was more common than dcSSc [32,33], while another study in African American showed that dcSSc was almost occurred in 50% [34]. This could be explained by the high frequency of ATA in our cohort and underscored the geographical differences and the ethnicity role in the disease etiology.

The frequency of the clinical features in our cohort were almost similar to other Arab countries cohort, like in Qatar and Egypt. Specifically, the Raynaud phenomena was found in 90.5% of our SScpatients, 85 % in Qatar patients and 97% in Egypt patients [26,28].

Additionally, we noticed that ILD development in our patients was 76.2%, whereas in European, Afro-Caribbean and Asian was ranged between thirty to fifty percentage [35]. This is a novel finding.

In our study, ILD was identified in 76.2% of patients, with a notably higher prevalence among those with diffuse cutaneous SSc (dcSSc), compared to in patients with the limited subtype (lcSSc). This pattern aligns with findings from Qatar, Egyptian and Spanish studies [26,28,30], which reported similar trends. In contrast, studies from Iran and Malaysia did not observe a significant difference in ILD prevalence between the two subtypes [29,36].

Regarding autoantibodies, ATA shows significant variation across different geographical regions. For instance, the ATA was found in approximately 66% of Qatari and 71% of Irani SSc patients. In contrast, its prevalence was much lower among European (15%), Afro-Caribbean (33%) and in Asian (43%) populations (11). In our study, ATA detected in 57.1% of patients. This relatively high frequency may contribute to the increased prevalence of ILD observed in out cohort. Ethnic background and environmental factors could also influenced shaping these immunological and clinical patterns.

In regard the ILD subtypes, our findings were similar to other studies [37], in which NSIP was the commonest.

ACA in all our patients with ILD was negative. Though, our study cohort contained small number of patients with positive ACA (n = 2), this finding may indicate that ACA is a protective predictor from ILD in Saudi. The distribution of ATA and ACA are varied between ethnicities. In European and Hispanic, ACA prevalence was higher than ATA, while in African American and Asian the ATA was the predominant [34,35]. This may contribute to the similarities and differences of the SSc clinical profile between different regions. This is first time to know that SSc occur in Saudi at early age with a mean of 33 year. This result was quite interesting as the mean age at diagnosis in Japanese, Thai and Malaysian SSc cohorts was not less than 40 year as well as in German cohort [38,39]. This study have few short comings including the small sample size and being a retrospective, despite that, it is the first cohort study describing the clinical and autoantibodies among Saudi population.

CONCLUSION

This first descriptive study of SSc in a Saudi cohort demonstrates younger age at diagnosis and high ILD prevalence compared with international populations. ATA showed a strong trend toward association with ILD, while ACA was absent among ILD cases, though patient numbers were too small for definitive inference. Larger, prospective, multicenter studies are urgently needed to validate these observations and support the development of national SSc registries.

Acknowledgement

The author expresses gratitude to King Saud Hospital, Qassim Cluster Research Centre for their substantial support and acknowledges all participating patients with appreciation.

Conflicts of Interest

The author declares no conflicts of interest.

Source of Funding

This research did not obtain any specific financing from public, commercial, or non-profit entities.

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